# In the Specification;

On pages 10 and 11, please replace the paragraph beginning on line 29 of page 10 with the following:

Figure 1 comprises Figures 1A through <u>1M[[1H]]</u>. The nucleotide sequence (SEQ ID NO: 1) of a cDNA encoding the human TANGO 202 protein described herein is listed in Figures 1A [[and 1B]]through 1D. The open reading frame (ORF; residues 34 to 1458; SEQ ID NO: 2) of the cDNA is indicated by nucleotide triplets, above which the amino acid sequence (SEQ ID NO: 3) of human TANGO 202 is listed. The nucleotide sequence (SEQ ID NO: 67) of a cDNA encoding the murine TANGO 202 protein described herein is listed in Figures 1E through 1I 1C, 1D, and 1E. The ORF (residues 81 to 1490; SEQ ID NO: 68) of the cDNA is indicated by nucleotide triplets, above which the amino acid sequence (SEQ ID NO: 69) of murine TANGO 202 is listed. An alignment of the amino acid sequences of human ("Hum."; SEQ ID NO: 3) and murine ("Mur."; SEQ ID NO: 69) TANGO 202 protein is shown in Figures 1J through 1K Figure 1F, wherein identical amino acid residues are indicated by ":" and similar amino acid residues are indicated by ".". Figure 1L [[1G]] is a hydrophilicity plot of human TANGO 202 protein, in which the locations of cysteine residues ("Cys") and potential Nglycosylation sites ("Ngly") are indicated by vertical bars and the predicted extracellular ("out"), intracellular ("ins"), or transmembrane ("TM") locations of the protein backbone is indicated by a horizontal bar. Figure 1M [[1H]] is a hydrophilicity plot of murine TANGO 202 protein.

On page 11, please replace the paragraph beginning on line 16 with the following:

Figure 2 comprises Figures 2A through 2Q. The nucleotide sequence (SEQ ID NO: 9) of a cDNA encoding the human TANGO 234 protein described herein is listed in Figures 2A through 2I[[2E]]. The ORF (residues 28 to 4386; SEQ ID NO: 10) of the cDNA is indicated by nucleotide triplets, above which the amino acid sequence (SEQ ID NO: 11) of human TANGO 234 is listed. Figure 2I[[2F]] is a hydrophilicity plot of human TANGO 234 protein. An alignment of the amino acid sequences of human TANGO 234 ("Hum"; SEQ ID NO: 11) and bovine WC1 ("WC1"; SEQ ID NO: 78) proteins is shown in Figures 2K through 2P 2G through

21, wherein identical amino acid residues are indicated by ":" and similar amino acid residues are indicated by ".". An alignment of the nucleotide sequences of an ORF encoding human TANGO 234 ("Hum"; SEQ ID NO: 10) and an ORF encoding bovine WC1 ("WC1"; SEQ ID NO: 79) proteins is shown in Figures 2Qi through 2Qxvii 2J through 2Q, wherein identical nucleotide residues are indicated by ":".

On pages 11 and 12, please replace the paragraph beginning on line 29 of page 11 with the following:

Figure 3 comprises Figures 3A through 3U[[3I]]. The nucleotide sequence (SEQ ID NO: 17) of a cDNA encoding the human TANGO 265 protein described herein is listed in Figures 3A through 3E[[, 3B, and 3C]]. The ORF (residues 32 to 2314; SEQ ID NO: 18) of the cDNA is indicated by nucleotide triplets, above which the amino acid sequence (SEQ ID NO: 19) of human TANGO 265 is listed. An alignment of the amino acid sequences of human TANGO 265 protein ("Hum."; SEQ ID NO: 19) and murine semaphorin B protein ("Mur."; SEQ ID NO: 70; GenBank Accession No. X85991) is shown in Figures 3F through 3H Figure 3D, wherein identical amino acid residues are indicated by ":" and similar amino acid residues are indicated by ".". In Figures 3I through 3T 3E, 3F, 3G, and 3H, an alignment of the nucleotide sequences of the cDNA encoding human TANGO 265 protein ("Hum."; SEQ ID NO: 17) and the nucleotide sequences of the cDNA encoding murine semaphorin B protein ("Mur."; SEQ ID NO: 71; GenBank Accession No. X85991) is shown. Figure 3U[[3I]] is a hydrophilicity plot of TANGO 265 protein.

On page 12, please replace the paragraph beginning on line 12 with the following:

Figure 4 comprises Figures 4A through 4J[[4G]]. The nucleotide sequence (SEQ ID NO: 25) of a cDNA encoding the human TANGO 273 protein described herein is listed in Figures 4A through 4C [[and 4B]]. The ORF (residues 135 to 650; SEQ ID NO: 26) of the cDNA is indicated by nucleotide triplets, above which the amino acid sequence (SEQ ID NO: 27) of human TANGO 273 is listed. The nucleotide sequence (SEQ ID NO: 72) of a cDNA encoding

the murine TANGO 273 protein described herein is listed in Figures <u>4D through 4G</u> <del>4C, and 4D</del>. The ORF (residues 137 to 652; SEQ ID NO: 73) of the cDNA is indicated by nucleotide triplets, above which the amino acid sequence (SEQ ID NO: 74) of murine TANGO 273 is listed. An alignment of the amino acid sequences of human ("Hum."; SEQ ID NO: 27) and murine ("Mur."; SEQ ID NO: 74) TANGO 273 protein is shown in Figure <u>4H[[4E]]</u>, wherein identical amino acid residues are indicated by ":" and similar amino acid residues are indicated by ".". Figure <u>4I[[4F]]</u> is a hydrophilicity plot of human TANGO 273 protein, and Figure <u>4J[[4G]]</u> is a hydrophilicity plot of murine TANGO 273 protein.

On pages 12 and 13, please replace the paragraph beginning on line 26 of page 12 with the following:

Figure 5 comprises Figures 5A through 5I[[5E]]. The nucleotide sequence (SEQ ID NO: 33) of a cDNA encoding the human TANGO 286 protein described herein is listed in Figures 5A through 5D [[and 5B]]. The ORF (residues 133 to 1497; SEQ ID NO: 34) of the cDNA is indicated by nucleotide triplets, above which the amino acid sequence (SEQ ID NO: 35) of human TANGO 286 is listed. Figure 5E[[5C]] is a hydrophilicity plot of TANGO 286 protein. An alignment of the amino acid sequences of human TANGO 286 ("286"; SEQ ID NO: 35) and BPI protein ("BPI"; SEQ ID NO: 38) protein is shown in Figures 5F through 5G Figure 5D, wherein identical amino acid residues are indicated by ":" and similar amino acid residues are indicated by ":". An alignment of the amino acid sequences of human TANGO 286 ("286"; SEQ ID NO: 35) and RENP protein ("RENP"; SEQ ID NO: 39) is shown in Figures 5H through 5I Figure 5E, wherein identical amino acid residues are indicated by ":" and similar amino acid residues are indicated by ":" and similar amino acid residues are indicated by ":" and similar amino acid residues are indicated by ":" and similar amino acid residues are indicated by ":" and similar amino acid residues are indicated by ":" and similar amino acid

On page 13, please replace the paragraph beginning on line 8 with the following:

Figure 6 comprises Figures 6A through 6H[[6E]]. The nucleotide sequence (SEQ ID NO: 45) of a cDNA encoding the human TANGO 294 protein described herein is listed in Figures 6A through 6C [[and 6B]]. The ORF (residues 126 to 1394; SEO ID NO: 46) of the

cDNA is indicated by nucleotide triplets, above which the amino acid sequence (SEQ ID NO: 47) of human TANGO 294 is listed. An alignment of the amino acid sequences of human TANGO 294 protein ("294"; SEQ ID NO: 47) and a known human lipase protein ("HLP"; SEQ ID NO: 75; GenBank Accession No. NP\_004181) is shown in Figures 6D through 6E Figure 6C, wherein identical amino acid residues are indicated by ":" and similar amino acid residues are indicated by ".". Figure 6F[[6D]] is a hydrophilicity plot of TANGO 294 protein. An alignment of the amino acid sequences of human TANGO 294 protein ("294"; SEQ ID NO: 47) and a known human lysosomal acid lipase protein ("LAL"; SEQ ID NO: 41) is shown in Figures 6G through 6H Figure 6E, wherein identical amino acid residues are indicated by ":" and similar amino acid residues are indicated by ":" and similar amino acid residues are indicated by ":"

On pages 13 and 14, please replace the paragraph beginning on line 22 of page 13 with the following:

Figure 7 comprises Figures 7A through <u>7F</u>[[7D]]. The nucleotide sequence (SEQ ID NO: 53) of a cDNA encoding the human INTERCEPT 296 protein described herein is listed in Figures 7A through 7C [[and 7B]]. The ORF (residues 70 to 1098; SEQ ID NO: 54) of the cDNA is indicated by nucleotide triplets, above which the amino acid sequence (SEQ ID NO: 55) of human INTERCEPT 296 protein is listed. Figure <u>7D</u>[[7C]] is a hydrophilicity plot of INTERCEPT 296 protein. An alignment of the amino acid sequences of human INTERCEPT 296 protein ("296"; SEQ ID NO: 55) and *C. elegans* C06E1.3 related protein ("CRP"; SEQ ID NO: 40) is shown in <u>Figures 7E through 7F Figure 7D</u>, wherein identical amino acid residues are indicated by ":" and similar amino acid residues are indicated by ":"

On pages 21 and 22, please replace the paragraph beginning on line 23 of page 21 with the following:

Figure <u>1L</u>[[1G]] depicts a hydrophilicity plot of human TANGO 202 protein. Relatively hydrophobic regions are above the dashed horizontal line, and relatively hydrophilic regions are below the dashed horizontal line. The hydrophobic region which corresponds to amino acid residues 1 to 19 of SEQ ID NO: 3 is the signal sequence of human TANGO 202 (SEQ ID NO:

4). The hydrophobic region which corresponds to amino acid residues 393 to 415 of SEQ ID NO: 3 is the transmembrane domain of human TANGO 202 (SEQ ID NO: 7). As described elsewhere herein, relatively hydrophilic regions are generally located at or near the surface of a protein, and are more frequently effective immunogenic epitopes than are relatively hydrophobic regions. For example, the region of human TANGO 202 protein from about amino acid residue 61 to about amino acid residue 95 appears to be located at or near the surface of the protein, while the region from about amino acid residue 395 to about amino acid residue 420 appears not to be located at or near the surface.

On page 22, please replace the paragraph beginning on line 19 with the following:

Figure 1M[[1H]] depicts a hydrophilicity plot of murine TANGO 202 protein. Relatively hydrophobic regions are above the dashed horizontal line, and relatively hydrophilic regions are below the dashed horizontal line. The hydrophobic region which corresponds to amino acid residues 1 to 19 of SEQ ID NO: 69 is the signal sequence of murine TANGO 202 (SEQ ID NO: 42). As described elsewhere herein, relatively hydrophilic regions are generally located at or near the surface of a protein, and are more frequently effective immunogenic epitopes than are relatively hydrophobic regions. For example, the region of murine TANGO 202 protein from about amino acid residue 61 to about amino acid residue 95 appears to be located at or near the surface of the protein, while the region from about amino acid residue 295 to about amino acid residue 305 appears not to be located at or near the surface

On page 23, please replace the paragraph beginning on line 5 with the following:

Human and murine TANGO 202 proteins exhibit considerable sequence similarity, as indicated herein in <u>Figures 1J through 1K Figure 1F</u>. <u>Figures 1J through 1K Figure 1F</u> depict[[s]] an alignment of human and murine TANGO 202 amino acid sequences (SEQ ID NOs: 3 and 69, respectively). In this alignment (made using the ALIGN software {Myers and Miller (1989) *CABIOS*, ver. 2.0}; pam120.mat scoring matrix; gap penalties -12/-4), the proteins are 76.5% identical. The human and murine ORFs encoding TANGO 202 are 87.4% identical, as

Practitioner's Docket No. <u>MBIO99-030RCEM (formerly 210147-006/6US)</u> USSN: 09/333,159 assessed using the same software and parameters.

On page 26, please replace the paragraph beginning on line 24 with the following:

TANGO 234 proteins and nucleic acid molecules encoding them comprise a family of molecules having certain conserved structural and functional features, as indicated by the conservation of amino acid sequence between human TANGO 234 protein and bovine WC1 protein, as shown in Figures 2K through 2P2G through 2I, and the conservation of nucleotide sequence between the ORFs encoding human TANGO 234 protein and bovine WC1 protein, as shown in Figures 2Qi through 2Qxvii2J through 2Q.

On page 34, please replace the paragraph beginning on line 17 with the following:

TANGO 234 is likely the human orthologue of ruminant protein WC1, and thus is involved with the physiological processes described above in humans. An alignment of the amino acid sequences of (human) TANGO 234 and bovine WC1 protein is shown in Figures 2K through 2P2G, 2H, and 2I. In this alignment (made using the ALIGN software {Myers and Miller (1989) CABIOS, ver. 2.0}; pam120.mat scoring matrix; gap penalties -12/-4), the proteins are 40.4% identical. An alignment of the nucleotide sequences of the ORFs encoding (human) TANGO 234 and bovine WC1 protein is shown in Figures 2Qi through 2Qxvii2J through 2Q. The two ORFs are 54.3% identical, as assessed using the same software and parameters.

On page 35, please replace the paragraph beginning on line 5 with the following:

Figure 2J[[2F]] depicts a hydrophilicity plot of human TANGO 234 protein. Relatively hydrophobic regions are above the dashed horizontal line, and relatively hydrophilic regions are below the dashed horizontal line. The hydrophobic region which corresponds to amino acid residues 1 to 40 of SEQ ID NO: 11 is the signal sequence of human TANGO 234 (SEQ ID NO: 12). The hydrophobic region which corresponds to amino acid residues 1360 to 1383 of SEQ ID NO: 11 is the transmembrane domain of human TANGO 234 (SEQ ID NO: 15). As described

elsewhere herein, relatively hydrophilic regions are generally located at or near the surface of a protein, and are more frequently effective immunogenic epitopes than are relatively hydrophobic regions. For example, the region of human TANGO 234 protein from about amino acid residue 225 to about amino acid residue 250 appears to be located at or near the surface of the protein, while the region from about amino acid residue 990 to about amino acid residue 1000 appears not to be located at or near the surface.

On page 41, please replace the paragraph beginning on line 26 with the following:

Human TANGO 265 protein exhibits considerable sequence similarity to murine semaphorin B protein (GenBank Accession no. X85991), as indicated herein in Figures 3F through 3H Figure 3D. Figures 3F through 3H Figure 3D depicts an alignment of the amino acid sequences of human TANGO 265 protein (SEQ ID NO: 19) and murine semaphorin B protein (SEQ ID NO: 76). In this alignment (pam120.mat scoring matrix, gap penalties £12/-4), the amino acid sequences of the proteins are 82.3% identical. Figures 3I through 3T 3E through 3H depict an alignment of the nucleotide sequences of cDNA encoding human TANGO 265 protein (SEQ ID NO: 77) and murine cDNA encoding semaphorin B protein (SEQ ID NO: 77). In this alignment (pam120.mat scoring matrix, gap penalties -12/-4), the nucleic acid sequences of the cDNAs are 76.2% identical. Thus, TANGO 265 is the human orthologue of murine semaphorin B and shares functional similarities to that protein.

On pages 42 and 43, please replace the paragraph beginning on line 20 of page 42 with the following:

Figure <u>3U</u>[[3I]] depicts a hydrophilicity plot of human TANGO 265 protein. Relatively hydrophobic regions are above the dashed horizontal line, and relatively hydrophilic regions are below the dashed horizontal line. The hydrophobic region which corresponds to amino acid residues 1 to 31 of SEQ ID NO: 19 is the signal sequence of human TANGO 265 (SEQ ID NO: 20). The hydrophobic region which corresponds to amino acid residues 684 to 704 of SEQ ID NO: 19 is the transmembrane domain of human TANGO 265 (SEQ ID NO: 23). As described

elsewhere herein, relatively hydrophilic regions are generally located at or near the surface of a protein, and are more frequently effective immunogenic epitopes than are relatively hydrophobic regions. For example, the region of human TANGO 265 protein from about amino acid residue 350 to about amino acid residue 375 appears to be located at or near the surface of the protein, while the region from about amino acid residue 230 to about amino acid residue 250 appears not to be located at or near the surface.

On page 50, please replace the paragraph beginning on line 12 with the following:

Figure 4I[[4F]] depicts a hydrophilicity plot of human TANGO 273 protein. Relatively hydrophobic regions are above the dashed horizontal line, and relatively hydrophilic regions are below the dashed horizontal line. The hydrophobic region which corresponds to amino acid residues 1 to 22 of SEQ ID NO: 27 is the signal sequence of human TANGO 273 (SEQ ID NO: 28). The hydrophobic region which corresponds to amino acid residues 61 to 81 of SEQ ID NO: 27 is the transmembrane domain of human TANGO 273 (SEQ ID NO: 31). As described also elsewhere herein, relatively hydrophilic regions are generally located at or near the surface of a protein, and are more frequently effective immunogenic epitopes than are relatively hydrophobic regions. For example, the region of human TANGO 273 protein from about amino acid residue 100 to about amino acid residue 120 appears to be located at or near the surface of the protein, while the region from about amino acid residue 130 to about amino acid residue 140 appears not to be located at or near the surface.

On page 51, please replace the paragraph beginning on line 17 with the following:

Figure 4J[[4G]] depicts a hydrophilicity plot of murine TANGO 273 protein. Relatively hydrophobic regions are above the dashed horizontal line, and relatively hydrophilic regions are below the dashed horizontal line. The hydrophobic region which corresponds to amino acid residues 1 to 22 of SEQ ID NO: 74 is the signal sequence of murine TANGO 273. As described elsewhere herein, relatively hydrophilic regions are generally located at or near the surface of a protein, and are more frequently effective immunogenic epitopes than are relatively hydrophobic

regions. For example, the region of murine TANGO 273 protein from about amino acid residue 100 to about amino acid residue 120 appears to be located at or near the surface of the protein, while the region from about amino acid residue 130 to about amino acid residue 140 appears not to be located at or near the surface.

On page 52, please replace the paragraph beginning on line 3 with the following:

Human and murine TANGO 273 proteins exhibit considerable sequence similarity, as indicated herein in Figure 4H[[4E]]. Figure 4H[[4E]] depicts an alignment of human and murine TANGO 273 protein amino acid sequences (SEQ ID NOs: 27 and 74, respectively). In this alignment (pam120.mat scoring matrix, gap penalties -12/-4), the proteins are 89.5% identical. Alignment of the ORF encoding human TANGO 273 protein and the ORF encoding murine TANGO 273 protein using the same software and parameters indicated that the nucleotide sequences are 84.1% identical.

On page 57, please replace the paragraph beginning on line 1 with the following:

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Figure 5E[[5C]] depicts a hydrophilicity plot of TANGO 286 protein. Relatively hydrophobic regions are above the dashed horizontal line, and relatively hydrophilic regions are below the dashed horizontal line. As described elsewhere herein, relatively hydrophilic regions are generally located at or near the surface of a protein, and are more frequently effective immunogenic epitopes than are relatively hydrophobic regions. For example, the region of human TANGO 286 protein from about amino acid residue 420 to about amino acid residue 435 appears to be located at or near the surface of the protein, while the region from about amino acid residue 325 to about amino acid residue 345 appears not to be located at or near the surface.

On page 63, please replace the paragraph beginning on line 16 with the following:

Figure 6F[[6D]] depicts a hydrophilicity plot of human TANGO 294 protein. Relatively hydrophobic regions are above the dashed horizontal line, and relatively hydrophilic regions are

below the dashed horizontal line. The hydrophobic region which corresponds to amino acid residues 1 to 33 of SEQ ID NO: 47 is the signal sequence of human TANGO 294 (SEQ ID NO: 49). The hydrophobic region which corresponds to amino acid residues 255 to 279 of SEQ ID NO: 47 is the predicted transmembrane domain of human TANGO 294 (SEQ ID NO: 51). As described elsewhere herein, relatively hydrophilic regions are generally located at or near the surface of a protein, and are more frequently effective immunogenic epitopes than are relatively hydrophobic regions. For example, the region of human TANGO 294 protein from about amino acid residue 130 to about amino acid residue 150 appears to be located at or near the surface of the protein, while the region from about amino acid residue 90 to about amino acid residue 100 appears not to be located at or near the surface.

## On page 64, please replace the paragraph beginning on line 11 with the following:

Human TANGO 294 protein exhibits considerable sequence similarity (i.e. about 75% amino acid sequence identity) to lingual and gastric lipase proteins of rat (Swissprot Accession no. P04634; Docherty et al. (1985) Nucleic Acids Res. 13:1891-1903), dog (Swissprot Accession no. P80035; Carriere et al. (1991) Eur. J. Biochem. 202:75-83), and human (Swissprot Accession no. P07098; Bernbaeck and Blaeckberg (1987) Biochim. Biophys. Acta 909:237-244), as assessed using the ALIGN v. 2.0 computer software using a pam12.mat scoring matrix and gap penalties of -12/-4. TANGO 294 is distinct from the known human lipase, as indicated in Figures 6D through 6E Figure 6C. Figures 6D through 6E Figure 6C depict[[s]] an alignment of the amino acid sequences of human TANGO 294 protein (SEQ ID NO: 47) and the known human lipase protein (SEQ ID NO: 75), as assessed using the same software and parameters. In this alignment (pam120.mat scoring matrix, gap penalties -12/-4), the amino acid sequences of the proteins are 49.8% identical. TANGO 294 also is distinct from the known human lysosomal acid lipase, as indicated in Figures 6G through 6H Figure 6E. Figures 6G through 6H Figure 6E depict[[s]] an alignment of the amino acid sequences of human TANGO 294 protein (SEQ ID NO: 47) and the known human lysosomal acid lipase protein (SEQ ID NO: 41). In this alignment (pam120.mat scoring matrix, gap penalties -12/-4), the amino acid sequences of the proteins are 56.9% identical.

On pages 68 and 69, please replace the paragraph beginning on line 25 of page 68 with the following:

Figure 7D[[7C]] depicts a hydrophilicity plot of INTERCEPT 296 protein. Relatively hydrophobic regions are above the dashed horizontal line, and relatively hydrophilic regions are below the dashed horizontal line. The hydrophobic regions which corresponds to amino acid residues 24 to 42, 51 to 70, 183 to 204, 211 to 227, and 250 to 271 of SEQ ID NO: 55 are the transmembrane domains of human INTERCEPT 296 (SEQ ID NOs: 59 through 63, respectively). As described elsewhere herein, relatively hydrophilic regions are generally located at or near the surface of a protein, and are more frequently effective immunogenic epitopes than are relatively hydrophobic regions. For example, the region of human INTERCEPT 296 protein from about amino acid residue 120 to about amino acid residue 140 appears to be located at or near the surface of the protein, while the region from about amino acid residue 95 to about amino acid residue 110 appears not to be located at or near the surface.

On page 69, please replace the paragraph beginning on line 13 with the following:

Figures 7E through 7F Figure 7D depict[[s]] an alignment of the amino acid sequences of human INTERCEPT 296 protein (SEQ ID NO: 55) and *Caenorhabditis elegans* C06E1.3 related protein (SEQ ID NO: 399). In this alignment (pam120.mat scoring matrix, gap penalties -12/-4), the amino acid sequences of the proteins are 26.8% identical. The *C. elegans* protein has five predicted transmembrane domains.

On page 90, please replace the paragraph beginning on line 7 with the following:

Preferred epitopes encompassed by the antigenic peptide are regions that are located on the surface of the protein, e.g., hydrophilic regions. Figures <u>1L, 1M, 2J, 3U, 4I, 4J, 5E, 6F and 7D1G, 1H, 2F, 3I, 4F, 4G, 5C, 6D, and 7C</u> are hydrophobicity plots of the proteins of the invention. These plots or similar analyses can be used to identify hydrophilic regions.